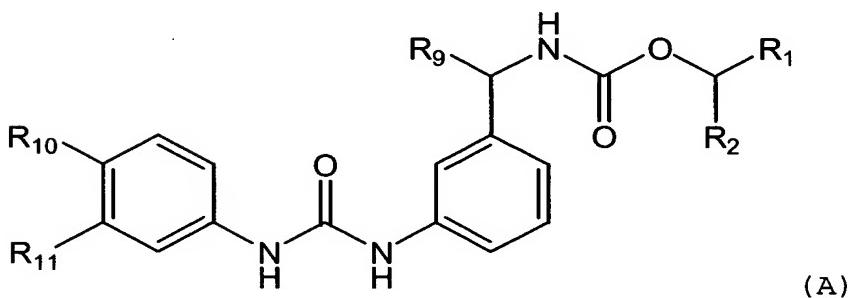


CLAIMS

We claim:

1. A composition comprising:
 - (a) an apoptosis inducing anti-cancer agent;
 - (b) a compound of formula (A):



wherein:

each of R₁ and R₂ is independently selected from hydrogen; -CF₃; -(C₁-C₆)-straight or branched alkyl; -(C₂-C₆)-straight or branched alkenyl or alkynyl; -(C₁-C₆)-straight or branched alkyl-R₇; -[(C₂-C₆)-straight or branched alkenyl or alkynyl]-R₇ or -R₇; and wherein at least one of R₁ or R₂ is -(C₁-C₆)-straight or branched alkyl-R₇; -[(C₂-C₆)-straight or branched alkenyl or alkynyl]-R₇ or -R₇

wherein up to 4 hydrogen atoms in any of said alkyl, alkenyl or alkynyl are optionally and independently replaced by R₃; and

wherein one or both of R₁ or R₂ are optionally esterified to form a prodrug; or

wherein R₁ and R₂ are alternatively taken together to form tetrahydrofuryl, wherein when R₉ is hydrogen, (R)-methyl, (R)-ethyl or (R)-hydroxymethyl, one hydrogen atom in said tetrahydrofuran is replaced by -OR₆

or -R₇, and wherein when R₉ is (S)-methyl, (S)-ethyl or (S)-hydroxymethyl, one hydrogen atom in said tetrahydrofuran is optionally replaced by -OR₆ or -R₇;

wherein when R₉ is hydrogen, (R)-methyl, (R)-ethyl or (R)-hydroxymethyl and each of R₁ and R₂ are independently hydrogen, unsubstituted -(C₁-C₆)-straight or branched alkyl, or unsubstituted -(C₂-C₆)-straight or branched alkenyl or alkynyl, then the portion of the compound represented by -CH(R₁)R₂ is a C₅-C₁₂ straight or branched alkyl, alkenyl or alkynyl;

each R₃ is independently selected from halo, CN, -OR₄, or -N(R₅)₂;

R₄ is selected from hydrogen, -(C₁-C₆)-straight or branched alkyl, -(C₂-C₆)-straight or branched alkenyl or alkynyl, -[(C₁-C₆)-straight or branched alkyl]-R₇, -[(C₂-C₆)-straight or branched alkenyl or alkynyl]-R₇, -C(O)-[(C₁-C₆)-straight or branched alkyl], -C(O)-[(C₂-C₆)-straight or branched alkenyl or alkynyl], -C(O)-[(C₁-C₆)-straight or branched alkyl]-N(R₈)₂, -C(O)-[(C₂-C₆)-straight or branched alkenyl or alkynyl]-N(R₈)₂, -P(O)(OR₈)₂, -P(O)(OR₈)(R₈), -C(O)-R₇, -S(O)₂N(R₅)₂, -[(C₁-C₆)-straight or branched alkyl]-CN, or -[(C₂-C₆)-straight or branched alkenyl or alkynyl]-CN;

each R₅ is independently selected from hydrogen, -(C₁-C₆)-straight or branched alkyl, -(C₂-C₆)-straight or branched alkenyl or alkynyl, -[(C₁-C₆)-straight or branched alkyl]-R₇, -[(C₂-C₆)-straight or branched alkenyl or alkynyl]-R₇, -[(C₁-C₆)-straight alkyl]-CN, -[(C₂-C₆)-straight or branched alkenyl or alkynyl]-CN, -[(C₁-C₆)-straight or branched alkyl]-OR₄, -[(C₂-C₆)-straight or branched alkenyl or alkynyl]-OR₄, -C(O)-(C₁-C₆)-straight or branched alkyl, -C(O)-[(C₂-C₆)-straight or branched

alkenyl or alkynyl], -C(O)-R₇, -C(O)O-R₇, -C(O)O-(C₁-C₆)-straight or branched alkyl, -C(O)O-[(C₂-C₆)-straight or branched alkenyl or alkynyl], -S(O)₂-(C₁-C₆)-straight or branched alkyl, or -S(O)₂-R₇; or two R₅ moieties, when bound to the same nitrogen atom, are taken together with said nitrogen atom to form a 3 to 7-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1 to 3 additional heteroatoms independently selected from N, O, S, S(O) or S(O)₂;

R₆ is selected from -C(O)-CH₃, -CH₂-C(O)-OH, -CH₂-C(O)-O-tBu, -CH₂-CN, or -CH₂-C≡CH;

each R₇ is a monocyclic or bicyclic ring system wherein in said ring system:

i. each ring comprises 3 to 7 ring atoms independently selected from C, N, O or S;

ii. no more than 4 ring atoms are selected from N, O or S;

iii. any CH₂ is optionally replaced with C(O);

iv. any S is optionally replaced with S(O) or S(O)₂;

each R₈ is independently selected from hydrogen or -[C₁-C₄]-straight or branched alkyl;

wherein in any ring system in said compound up to 3 hydrogen atoms bound to the ring atoms are optionally and independently replaced with halo, hydroxy, nitro, cyano, amino, (C₁-C₄)-straight or branched alkyl; O-(C₁-C₄)-straight or branched alkyl, (C₂-C₄)-straight or branched alkenyl or alkynyl, or O-(C₂-C₄)-straight or branched alkenyl or alkynyl; and

wherein any ring system is optionally benzofused;

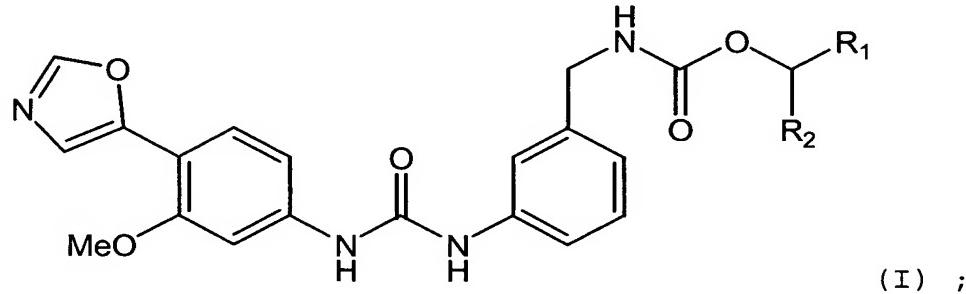
R₉ is selected from hydrogen, (R)-methyl, (S)-methyl, (R)-ethyl, (S)-ethyl, (R)-hydroxymethyl or (S)-hydroxymethyl;

R₁₀ is selected from -C=N or 5-oxazolyl; and

R₁₁ is selected from halo, -O-(C₁-C₃) straight alkyl, or -O-(C₂-C₃) straight alkenyl or alkynyl;

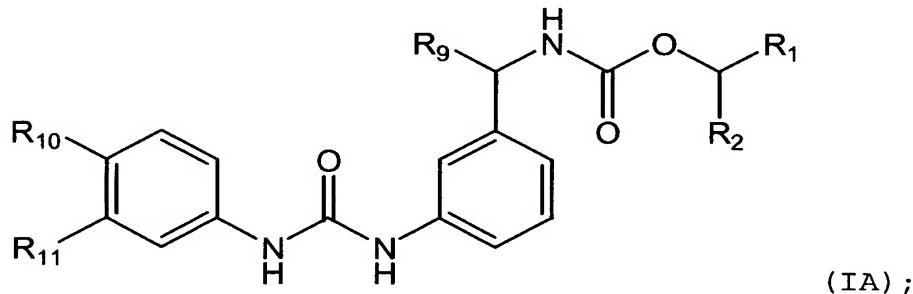
(c) a pharmaceutically acceptable carrier.

2. The composition according to claim 1, wherein said compound has the formula (I):



wherein R₁ and R₂ are as defined in claim 1.

3. The composition according to claim 1, wherein said compound has the formula (IA):



wherein R₉ is selected from (R)-methyl, (S)-methyl, (R)-ethyl, (S)-ethyl, (R)-hydroxymethyl or (S)-hydroxymethyl; and

R₁ and R₂ are as defined in claim 1.

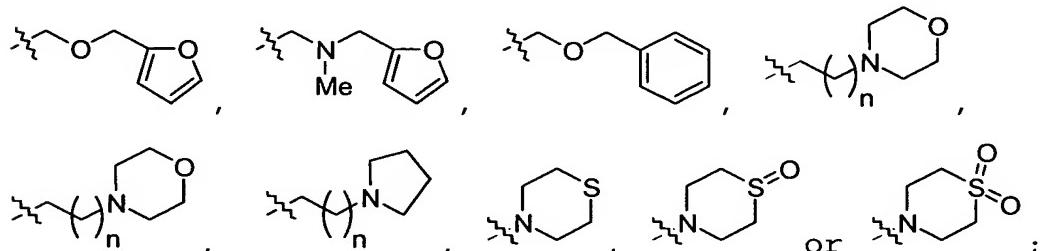
4. The composition according to claim 3,
wherein R₉ is selected from (S)-methyl, (S)-ethyl, or (S)-
hydroxymethyl methyl.

5. The composition according to claim 4,
wherein R₉ is (S)-methyl.

6. The composition according to claim 3,
wherein R₁₁ is selected from O-methyl, O-ethyl or O-
isopropyl.

7. The composition according to claim 1,
wherein:

at least one of R₁ or R₂ is selected from hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl, n-pentyl, phenyl, pyridyl, -CH₂OCH₃, -CH₂CN, -CH₂OCH₂CH₂CN, -CH₂C(CH₃)₂CH₂CH₂CN, -CH₂C(CH₂CH₃)₂CH₂CH₂CN, -CH₂CH₂CN, -CH₂N(CH₂CH₂CN)₂, -CH₂N(CH₃)CH₂CH₂CN, -CH(NH₂)CH₂CN, -CH₂Cl, -CH₂OH, -CH₂CH₂OH, -CH₂CH₂OH, -CH₂CH₂CH₂CH₂OH, -CH₂CH₂OC(O)CH₃, -CH₂CH₂OC(O)CH₂NH₂, -CH₂CH₂NHCH₃, -CH₂CH₂N(CH₃)₂, -CH₂N(CH₂CH₃)₂, -CH₂CH₂N(CH₂CH₃)₂, -CH₂CH₂CH₂N(CH₃)₂, -CH₂CH₂CH₂N⁺(CH₃)₃, -CH₂OCH₂CH(CH₃)₂, -CH₂CH₂N(CH₃)C(O)OC(CH₃)₃, -CH₂N(CH₂CH₂CN)CH₂CH(CH₃)₂, -CH(CH₂CN)N(CH₃)₂, -CH₂CH(CH₂CN)NHC(O)OC(CH₃)₃,



wherein n is 0 or 1.

8. The composition according to claim 2,

wherein R₁ and R₂ are taken together to form a 3-tetrahydrofuryl moiety that is substituted at the 5 position by -OR₆.

9. The composition according to claim 3, wherein one of R₁ or R₂ is selected from hydrogen, ethyl or phenyl; and the other of R₁ or R₂ is selected from -CH₂OH, -CH₂CN, -CH₂CH₂CN or CH₂N(CH₂CH₃)₂; or wherein R₁ and R₂ are taken together to form a 3-tetrahydrofuryl moiety.

10. The composition according to claim 1, wherein said compound is selected from any one of compounds 1 to 187 in Table 1.

11. The composition according to claim 10, wherein said compound is selected from any one of compounds 1, 23, 26, 27, 29, 32, 76, 80, 87, 89, 98, 101, 103, 104, 106, 108, 110, 157, 163, 169, 171, 181, 185, 186 or 187 in Table 1.

12. The composition according to any one of claims 1-11, wherein said apoptosis inducing anti-cancer agent is an anti-metabolite.

13. The composition according to claim 12, wherein said anti-metabolite is selected from cytarabine, fludarabine, 5-fluro-2'-deoxyuridine, gemcitabine, hydroxyurea, or methotrexate.

14. The composition according to claim 13,

wherein said anti-metabolite is selected from cytarabine, fludarabine, or 5-fluro-2'-deoxyuridine.

15. The composition according to claim 14, wherein said anti-metabolite is selected from fludarabine or cytarabine.

16. The composition according to claim 15, wherein said anti-metabolite is fludarabine.

17. The composition according to claim 13, wherein said anti-metabolite is hydroxyurea or methotrexate.

18. The composition according to claim 17, wherein said anti-metabolite is methotrexate.

19. The composition according to any one of claim 12-18, wherein said compound is selected from compound No. 169 and 181.

20. A method for inhibiting tumors and cancer in a mammal comprising the step of administrating to said mammal a composition according to any one of claims 1-19.

21. The method according to claim 20, wherein said method is useful to treat or prevent lymphoma, leukemia and related disorders, myelodysplastic syndrome, metastatic melanoma, and other forms of cancer.